5.07 FINERENONE, Tablet 10 mg, Tablet 20 mg, Kerendia®, Bayer Australia Ltd.

1 Purpose of submission

1.1 The Category 2 submission requested a Section 85 (General Schedule) PBS listing for finerenone for the treatment of diabetic kidney disease. The PBAC has not previously considered finerenone for any indication.

1.2 Listing was requested on the basis of a cost-effectiveness analysis versus placebo (standard of care).

Table 1: Key components of the clinical issue addressed in the submission (as stated in the submission)

Component	Description
Population	Patients with type 2 diabetes mellitus and chronic kidney disease with albuminuria
Intervention	Finerenone 10 mg or 20 mg oral tablets once daily with dose titration based on renal function and serum potassium levels. To be used in conjunction with standard of care including an ACEi or ARB (unless contraindicated).
Comparator	Placebo, to be used in conjunction with standard of care including an ACEi or ARB (unless contraindicated). Standard of care also comprises SGLT2i indicated for chronic kidney disease.
Outcomes	Delay kidney disease progression (including progression to kidney failure), reduce cardiovascular events and increase survival.
Clinical claim	The submission claimed that finerenone plus standard care is superior in terms of efficacy and 'comparable' in terms of safety compared to placebo plus standard care.

Source: Table 10 (p3), and pp iv-v of the submission.
Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; SGLT2i, sodium-glucose cotransporter inhibitor.

2 Background

Registration status

2.1 Finerenone was approved by the TGA on 25 November 2021 to 'delay progressive decline of kidney function in adults with chronic kidney disease associated with Type 2 diabetes (with albuminuria), in addition to standard of care'. At the time of PBAC consideration, the TGA was evaluating an application to amend the finerenone indication: 'to delay progressive decline of kidney function and to reduce the risk of cardiovascular mortality and morbidity in adults with chronic kidney disease associated with Type 2 diabetes (with albuminuria), in addition to standard of care'. The TGA outcome for this additional wording was not available at the time of PBAC consideration.

For more detail on PBAC's view, see section 7 PBAC outcome.

3 Requested listing

3.1 Suggestions and additions proposed by the secretariat are added in italics and suggested deletions are crossed out with strikethrough. The pre-PBAC response agreed with the secretariat's proposed revisions to the restriction shown in the table below, which is based on the ESC's advice discussed in paragraphs 3.3 to 3.7.

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Dispensed price for maximum quantity**	**Available brands**
FINERENONE						
finerenone 10 mg tablet, 28	NEW	1	28	5	$	Kerendia
finerenone 20 mg tablet, 28	NEW	1	28	5	$	Kerendia

Restriction Summary [new] / Treatment of Concept: [new]	
Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners ☒Nurse practitioners
	Restriction type: ☒Authority Required (Streamlined) [new/existing code]
	Administrative Advice: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.
	Condition: Chronic kidney disease with Type 2 diabetes
	Indication: Chronic kidney disease with Type 2 diabetes
	Clinical criteria:
	Patient must have a diagnosis of chronic diabetic kidney disease, defined as abnormalities of kidney structure or function present for 3 months or more, prior to initiating treatment with this drug,
	AND
	Clinical criteria:
	Patient must not have known significant non-diabetic renal disease, prior to initiating treatment with this drug.
	AND
	~~Patient must meet the following urinary albumin-to-creatinine ratio and estimated GFR eligibility criteria to substantiate the diagnosis of kidney disease, prior to initiating treatment with this drug:~~ ~~• UACR of 30-299 mg/g (3.39-33.9 mg/mmol) and eGFR of 25-90 mL/min/1.71 m^2 or~~ ~~• UACR of ≥300 mg/g (33.9 mg/mmol) and eGFR of ≥25 mL/min/1.71 m^2~~ *Patient must have (i) an estimated glomerular filtration rate of between 25 and 90 mL/min/1.73 m^2 inclusive, and (ii) a urinary albumin-to-creatinine ratio of 30 mg/g (3.39 mg/mmol) or greater, prior to initiating treatment with this drug,* *OR* *Patient must have (i) an estimated glomerular filtration rate of 90 mL/min/1.73 m^2 or greater, and (ii) a urinary albumin-to-creatinine ratio of 300 mg/g (33.9 mg/mmol) or greater, prior to initiating treatment with this drug,*
	~~**AND**~~
	~~**Clinical criteria:**~~
	~~Diagnosed Type 2 diabetes mellitus~~
	AND
	Clinical criteria:

	~~Patient must not progress to renal replacement therapy, defined as dialysis or transplant while on this drug.~~ *Patient must discontinue treatment with this drug prior to initiating renal replacement therapy, defined as dialysis or kidney transplant,*
	AND
	Clinical criteria:
	~~Patient must receive treatment in combination with the maximum tolerated dose of an ACE inhibitor; OR~~ ~~Patient must receive treatment in combination with the maximum tolerated dose of an angiotensin II antagonist, unless medically contraindicated~~ *The treatment must be in combination with the maximum tolerated dose of one of the following, unless medically contraindicated: (i) an ACE inhibitor or (ii) an angiotensin II antagonist.*
	AND
	Clinical criteria:
	Patient must not be receiving treatment with another selective nonsteroidal mineralocorticoid receptor antagonist, a renin inhibitor or a potassium-sparing diuretic.
	AND
	Clinical criteria:
	Patient must not have established heart failure with reduced ejection fraction with an indication for treatment with a mineralocorticoid receptor antagonist.
	Prescribing Instructions: Patient must be stabilised on either (i) an ACE inhibitor or (ii) an angiotensin II antagonist for a period of 4 weeks prior to initiation of combination therapy with this drug, unless medically contraindicated.
	Caution: *Serum electrolytes should be checked regularly*

3.2 The proposed PBS restriction for finerenone was narrower than the TGA indication as it limited eligibility to patients who have had prior therapy with an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin II receptor blockers (ARB), unless contraindicated, and included specific requirements in terms of renal function and albuminuria.

3.3 The ESC noted that the requested renal function and albuminuria criteria did not align precisely with the inclusion criteria in the pivotal trials, due to FIDELIO-DKD targeting slightly more severe chronic kidney disease (CKD) than FIGARO-DKD and FIDELIO-DKD requiring retinopathy in the milder proteinuric group, as shown in Table 2.

Table 2: Comparison of renal function and albuminuria criteria in requested PBS listing and key trials

Requested PBS listing	UACR of 30-299 mg/g (3.39-33.9 mg/mmol) and eGFR of 25-90 mL/min/1.73 m^2 or UACR of ≥ 300 mg/g (33.9 mg/mmol) and eGFR of ≥ 25 mL/min/1.73 m^2
FIDELIO-DKD	UACR of ≥ 30 mg/g (≥ 3.4 mg/mmol) but < 300 mg/g (< 33.9 mg/mmol) and eGFR ≥ 25 but < 60 mL/min/1.73 m^2 and presence of diabetic retinopathy in the medical history or UACR of ≥ 300 mg/g (≥ 33.9 mg/mmol) and eGFR ≥ 25 but < 75 mL/min/1.73 m^2
FIGARO-DKD	UACR of ≥ 30 mg/g (≥ 3.4 mg/mmol) but <300 mg/g (< 33.9 mg/mmol) and eGFR ≥ 25 but ≤ 90 mL/min/1.73 m^2 or UACR of ≥ 300 mg/g (≥ 33.9 mg/mmol) and eGFR ≥ 60 mL/min/1.73 m^2

Source: Table 18 (p22) and Table 29 (pp42-43) of the submission

3.4 The ESC advised that the eGFR parameter should precede the UACR parameter in each criterion of the proposed listing. For the first criterion (eGFR of 25-90 mL/min/1.73 m2

and UACR of 30-299 mg/g (3.39-33.9 mg/mmol)), the ESC advised that the UACR parameter could be simplified to UACR greater than 30 mg/g (3.39 mg/mmol). For the second criterion (eGFR ≥ 25 mL/min/1.73 m2 and UACR ≥ 300mg/g (≥ 33.9mg/mmol)), the ESC advised that the eGFR parameter should be simplified to be eGFR greater than 90 mL/min/1.73 m2, as this would remove the substantial overlap between the criteria.

3.5 The ESC also noted that the proposed PBS restriction is broader than the key trial populations which specifically excluded patients with Class II to IV heart failure with reduced ejection fraction (HFrEF) and also specifically excluded concomitant therapy with eplerenone, spironolactone, any renin inhibitor or a potassium-sparing diuretic (the TGA Product Information also states that concomitant use of these therapies should be avoided). The availability of finerenone in patient populations already being treated with another MRA may result in patients switching therapies (as these therapies should not be used in combination) with uncertain incremental benefits/harms. The ESC advised that to avoid prescriber confusion and uncertain cost-effectiveness the restriction should explicitly exclude patients taking renin inhibitors, potassium-sparing diuretics, or other MRAs and patients with established HFrEF and an indication for an MRA.

3.6 The ESC noted that time to kidney failure was a component of clinical endpoints in the pivotal trials, and was defined as end-stage renal disease (ESRD) or a sustained eGFR < 15 mL/min/1.73 m2 confirmed by a second measurement at ≥ 4 weeks after the initial measurement. The ESC also noted that the risk of hyperkalaemia increases substantially for patients with eGFR < 15 mL/min/1.73 m2.

3.7 The ESC advised that it was appropriate for the restriction to require patients to have sustained evidence of CKD and to exclude patients with known significant non-diabetic renal disease, as it considered that this was consistent with the key trial eligibility criteria.

3.8 The proposed restriction did not include any clinical criteria regarding the use of diabetic medications. It was unclear to the evaluation whether this was appropriate given the proposed second-line role for finerenone in patients already receiving standard care (lifestyle advice, ACEi or ARB treatment and standard diabetes management). The importance of glucose control in the reduction of cardiorenal complications in diabetic kidney disease is well established and recent guideline recommendations indicate that optimisation of specific medications (SGTL2 inhibitors and GLP1 analogues) may further reduce complications in the target population (2020 Kidney Health Australia CKD Management in Primary Care Handbook, 2020 RACGP Management of Type 2 Diabetes Handbook, 2020 Kidney Disease Improving Global Outcomes Guidelines; 2022 American Diabetes Association Chronic Kidney Disease Guidelines, 2019 European Society of Cardiology/ European Association for the Study of Diabetes Guidelines on diabetes, pre-diabetes, and cardiovascular diseases). The Pre-Sub-Committee Response (PSCR) noted that management of glycaemic control in the key clinical trials followed the recommendation of local guidelines.

For more detail on PBAC's view, see section 7 PBAC outcome.

4 Population and disease

4.1 Type 2 diabetes mellitus is a common chronic disease (affecting over one million Australians) characterised by high blood glucose levels due to inadequate insulin production and/or inadequate response of cells to insulin. Diabetic nephropathy is a common complication of diabetes with approximately 1 in 3 adults with diabetes having CKD. CKD is characterised by the gradual loss of kidney function over time which decreases the ability to filter waste products from the blood. The earlier stages of this condition are frequently asymptomatic but can progress over time with a variety of symptoms (e.g. tiredness, frequent urination, nausea and vomiting, itchiness, swelling) and complications (e.g. hypertension, heart failure and cardiomyopathy, anaemia, mineral and bone disorders, electrolyte abnormalities). At later stages, when the kidneys can no longer function on their own, people need kidney replacement therapy such as dialysis or kidney transplant to survive.

4.2 Finerenone is a non-steroidal mineralocorticoid receptor antagonist that belongs to a broader group of drugs classified as potassium-sparing diuretics. Finerenone has a similar mechanism of action to existing steroidal mineralocorticoid receptor antagonists (such as spironolactone and eplerenone) and works by inhibiting mineralocorticoid receptor-mediated sodium reabsorption as well as mineralocorticoid receptor overactivation which may contribute to fibrosis and inflammation in both epithelial (kidney) and nonepithelial (heart and blood vessel) tissues. In contrast to existing steroidal agents, the submission noted that finerenone has no relevant affinity for androgen, progesterone, oestrogen and glucocorticoid receptors and does not cause sex hormone-related adverse events (e.g. gynaecomastia).

4.3 The submission positioned finerenone as an additional line of therapy after lifestyle advice, ACEi or ARB treatment and standard diabetes management in patients with diabetic kidney disease who have persistent high-to-very high albuminuria levels. At the time of PBAC consideration, the only major clinical guidelines which specifically included finerenone were the 2022 American Diabetes Association Chronic Kidney Disease Guidelines, which position it as a treatment option in patients who are at increased risk of cardiovascular events or chronic kidney disease progression or are unable to use an SGLT2 inhibitor. The March 2022 public review draft of the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease also positioned nonsteroidal MRAs (i.e. finerenone) as 'most appropriate for patients with T2D [type 2 diabetes] who are at high risk of CKD progression and cardiovascular events, as demonstrated by persistent albuminuria despite other standard of care therapies' and state that 'in general, SGLTi should be initiated prior to adding a nonsteroidal MRA for treatment of T2D and CKD'.

4.4 The submission claimed that there is a clinical need for additional treatment options in diabetic kidney disease with different mechanisms of action that complement existing treatment strategies.

For more detail on PBAC's view, see section 7 PBAC outcome.

5 Comparator

5.1 The submission nominated placebo (standard of care) as the main comparator. The main argument provided in support of this nomination was that finerenone offers an alternative mechanism of action and would be used in addition to the current standard of care for diabetic kidney disease (ACEi or ARB with anti-diabetic agents used for glycaemic control) and therefore would not replace existing therapies.

5.2 The submission argued against SGLT2 inhibitors (such as dapagliflozin and empagliflozin) being considered as comparators on the basis that, while they are recommended for the management of diabetic kidney disease in current treatment guidelines, they are also established anti-diabetic agents used for glycaemic control and are therefore more likely to be considered as part of standard of care. The ESC considered that this argument appeared reasonable, advising that most patients would receive an SGLT2 inhibitor prior to being considered for finerenone.

5.3 The submission did not consider steroidal MRAs (such as spironolactone and eplerenone) as potential comparators. This evaluation considered that this may be reasonable given that there is a lack of data for their use in diabetic kidney disease and they are not identified as recommended treatment options in current treatment guidelines. However, the evaluation also noted that a substantial proportion of patients with diabetic kidney disease are likely to also have comorbid heart failure and/or treatment-resistant essential hypertension for which steroidal MRAs are recommended treatment options and therefore the listing of finerenone has the potential to displace these therapies in this subgroup of patients. The ESC considered that the restriction should explicitly exclude patients on other MRAs or patients with established HFrEF and an indication for an MRA, which would prevent this displacement.

For more detail on PBAC's view, see section 7 PBAC outcome.

6 Consideration of the evidence

Sponsor hearing

6.1 The sponsor requested a hearing for this item. The clinician discussed the burden of disease, the mechanism of action of finerenone, outlined the pivotal clinical trials, and how finerenone would be used in clinical practice. The clinician stated that finerenone has a complimentary mechanism of action to the current standard care medications (ACE inhibitor or ARB and SGLT2 inhibitor) and outlined the clinical benefits associated with combination therapy. The clinician also outlined the rates of hyperkalaemia

reported in the clinical trials and considered that the protocols utilised in the clinicals trials to reduce the risk of hyperkalaemia would be manageable in clinical practice.

Consumer comments

6.2 The PBAC noted and welcomed the input from health care professionals (2) and one organisation via the Consumer Comments facility on the PBS website. The comments from health professionals discussed the current lack of effective treatments that target both inflammation and fibrosis for managing patients with diabetic kidney disease. The health professionals emphasised that finerenone offered health benefits to patients with a manageable side effect profile and outlined the potential savings to the health system that may result from reducing the costs associated with treating diabetes-related complications.

6.3 The PBAC noted the advice received from Diabetes Australia highlighting the epidemiology of diabetic kidney disease and commenting that the use of finerenone may improve quality of life and health outcomes for people living with diabetes and reduce hospitalisation costs associated with treating diabetes-related complications. The PBAC considered that the evidence provided in the submission was only marginally supportive of this advice and that the magnitude of benefit with finerenone over standard care was likely modest at best.

Clinical trials

6.4 The submission was based on 2 head-to-head randomised trials comparing finerenone to placebo in diabetic kidney disease patients (FIDELIO-DKD, FIGARO-DKD) as well as a pre-specified pooled analysis of individual patient data from both trials (FIDELITY).

6.5 Details of the included studies are provided in Table 3.

Table 3: Studies and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
FIDELIO-DKD	Bayer (2020). Efficacy and Safety of Finerenone in Subjects With Type 2 Diabetes Mellitus and Diabetic Kidney Disease	Internal study report
	Bakris et al (2019). Design and baseline characteristics of the finerenone in reducing kidney failure and disease progression in diabetic kidney disease trial.	American Journal of Nephrology 50: 333-344.
	Bakris et al (2020). Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes.	New England Journal of Medicine 383: 2219-2229.
	Filippatos et al (2021). Finerenone and Cardiovascular Outcomes in Patients with Chronic Kidney Disease and Type 2 Diabetes.	Circulation 143: 540-552.
	Filippatos et al (2021b). Finerenone Reduces New-Onset Atrial Fibrillation in Patients With Chronic Kidney Disease and Type 2 Diabetes.	Journal of the American College of Cardiology 78: 142-152.
	Agarwal et al (2022). Hyperkalemia Risk with finerenone: Results from the FIDELIO-DKD Trial.	Journal of the American Society of Nephrology 33: 225–237
	Rossing et al (2021). Finerenone in Predominantly Advanced CKD and Type 2 Diabetes With or Without Sodium-Glucose Cotransporter-2 Inhibitor Therapy[a]	Kidney International Reports 7: 36-45.
	Filippatos et al (2022). Finerenone in patients with CKD and T2D with and without heart failure: A prespecified subgroup analysis of the FIDELIO-DKD trial[a]	European Journal of Heart Failure doi: 10.1002/ejhf.2469
	Rossing et al (2022). Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes According to Baseline HbA1c and Insulin Use: An Analysis From the FIDELIO-DKD Study[a]	Diabetes Care doi: 10.2337/dc21-1944
	Rossing et al (2022b). Efficacy and safety of finerenone in patients with chronic kidney disease and type 2 diabetes by GLP1RA treatment: A subgroup analysis from the FIDELIO-DKD trial[a]	Diabetes, Obesity & Metabolism 24: 125-134.
FIGARO-DKD	Bayer (2021). Efficacy and safety of finerenone in subjects with type 2 diabetes mellitus and the clinical diagnosis of diabetic kidney disease	Internal study report
	Ruilope et al (2019). Design and baseline characteristics of the finerenone in reducing cardiovascular mortality and morbidity in diabetic kidney disease trial.	American Journal of Nephrology 50: 345-356.
	Pitt et al (2021). Cardiovascular events with finerenone in kidney disease and Type 2 diabetes[a]	New England Journal of Medicine 385: 2252-2263.
	Filippatos et al (2022). Finerenone reduces risk of incident heart failure in patients with chronic kidney disease and Type 2 diabetes: analyses from the FIGARO-DKD trial[a]	Circulation 145: 437-447.
FIDELITY	Bayer (2021). Integrated analysis of FIDELIO-DKD and FIGARO-DKD	Internal study report
	Agawal et al (2022). Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis	European Heart Journal 43: 474-484.

Source: Table 24 (pp30-31) of the submission
Note: Abstracts of studies with full publications are not presented
[a] Publications identified during evaluation

6.6 At the time of PBAC consideration, there were 2 ongoing additional trials comparing finerenone with placebo for the treatment of preserved fraction heart failure (FINEARTS-HF, estimated completion May 2024) and treatment of non-diabetic kidney disease (FINE-CKD, estimated completion December 2025).

6.7 The key features of the included studies are summarised in Table 4 below.

Table 4: Key features of the included studies

Trial	N	Design/ duration	Risk of bias	Patient population	Outcomes	Use in modelled evaluation
FIDELIO-DKD	5,734	MC, R, DB, PC Event-driven trial Mean 32 month duration	Low	Patients with diabetic kidney disease (predominantly advanced disease) receiving ACEi or ARB monotherapy as part of standard of care	Cardiorenal outcomes, biomarkers, quality of life and adverse events	Not used
FIGARO-DKD	7,437	MC, R, DB, PC Event-driven trial Mean 40 month duration	Low	Patients with diabetic kidney disease receiving ACEi or ARB monotherapy as part of standard of care	Cardiorenal outcomes, biomarkers, quality of life and adverse events	Not used
FIDELITY	13,026	Pooled analysis of individual patient data from FIDELIO-DKD and FIGARO-DKD	Low	Patients with diabetic kidney disease receiving ACEi or ARB monotherapy as part of standard of care	Cardiorenal outcomes, biomarkers, quality of life and adverse events	Baseline risk, treatment effects, utility values

Source: Section 2.3.1 (pp36-40) and Section 2.4 (pp41-57) of the submission
Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; DB, double-blind; MC, multicentre; PC, placebo-controlled; R, randomised

6.8 The submission presented a comparison between the trial populations and an Australian diabetic kidney disease population. The Australian population identified in the submission was based on a sponsor-commissioned analysis of OneNil electronic medical records database, from which the submission attempted to identify a FIDELITY-like population. This comparison suggested substantial differences in a number of key characteristics that would affect the underlying risk of cardiorenal events such as: baseline eGFR (trial 39.9% versus 57% with eGFR > 60 mL/min/1.73m^2), baseline albuminuria (trial 66.7% versus 23% with UACR > 300 mg/g), history of cardiovascular disease (trial 45.6% versus 15%), use of ACEi/ARBs (trial 99.8% versus 42%) and use of SGLT2 inhibitors (trial 6.7% versus 14%). The evaluation had considered that the population selected from the OneNil database was at much lower risk of cardiorenal complications compared to the trial populations, although the ESC noted that the impact of the different baseline characteristics would be bidirectional. The rules applied to the OneNil database were inadequate to identify an Australian population who have diabetic kidney disease with persistent albuminuria despite standard-of-care therapy (for example, ESC was particularly concerned that the high numbers of patients not treated with ACEi/ARB would not reflect the target population, with only a small number likely to be contraindicated) and therefore this comparison was of limited value. Overall, the ESC considered that the population selected from the OneNil database was unlikely to be adequately representative of the proposed Australian PBS population.

6.9 The trials used a quota sampling approach which limited the proportion of the trial population with certain patient characteristics (e.g. capping patients without cardiovascular disease). The effect of this approach was to alter the distribution of

patients across the diabetic kidney disease spectrum and to distort the baseline population risk and the rate of cardiorenal events in the trials. The PSCR considered that the screening process did not alter the risk profile of the patient population to such an extent that the clinical trials would lack applicability to the proposed PBS population. It also suggested that the finerenone treatment effect is independent of cardiovascular characteristics (based on pre-specified subgroup analyses and the lack of significant interaction between cardiovascular disease at baseline and clinical outcomes). The ESC considered that the quota sampling approach did not affect the internal validity of the observed treatment effects and could be interpreted similarly to stratifying patients based on certain baseline characteristics. However, altering the baseline risk profile of the patient population had significant implications for the economic model (see Table 13).

6.10 The finerenone trials were conducted prior to recent guideline recommendations for the use of SGLT2 inhibitors and GLP1 analogues to reduce the risk of cardiovascular and renal complications in patients with diabetic kidney disease (2020 Kidney Health Australia CKD Management in Primary Care Handbook; 2020 RACGP Management of Type 2 Diabetes Handbook; 2020 Kidney Disease Improving Global Outcomes Guidelines; 2022 American Diabetes Association Chronic Kidney Disease Guidelines; 2019 European Society of Cardiology/ European Association for the Study of Diabetes Guidelines on diabetes, pre-diabetes, and cardiovascular diseases). The baseline use of these therapies in the clinical trials was low, although progressively increased during the course of the trial likely reflecting changing clinical practice. Dapagliflozin, a SGLT2 inhibitor, was recommended for PBS listing for patients with CKD at the March 2022 PBAC meeting. The ESC agreed with the evaluation that a higher use of SGLT2 inhibitors and GLP1 analogues in clinical practice would likely reduce the underlying risk of events compared to the trial populations.

6.11 The risk of hyperkalaemia was managed in the clinical trials through a combination of careful patient selection, intensive monitoring and dose adjustments (down-titrations and dose interruptions) as well as increased use of potassium lowering agents. The PSCR claimed that the finerenone Product Information (PI) and routine clinical monitoring would be sufficient for Australian clinicians to manage the risk of hyperkalaemia in line with the pivotal clinical trials. However, the ESC considered it unlikely that the risk management measures used in the trials would be representative of clinical practice. Additionally, while the majority of patients in the clinical trials were using the higher 20 mg finerenone dose strength, the ESC considered that it is unclear how often physicians would up titrate to the higher finerenone dose due to concerns over the risk of hyperkalaemia and whether suboptimal dosing of finerenone may result. The PBAC noted that the rates of screening failure (assuming hyperkalaemia was the most common cause) were higher than expected in both trials (61.6% in FIGARO-CKD and 58.8% in FIDELIO-CKD versus 50% assumed), which reinforced concerns around patient selection outside of the clinical trial setting.

Comparative effectiveness

6.12 Composite cardiovascular events reported with finerenone and placebo treatment in the FIDELIO-DKD and FIGARO-DKD trials are summarised in Table 5 below. This was the primary outcome of the FIGARO-DKD trial and a key secondary outcome of the FIDELIO-DKD trial. The incidence of component outcomes reported in the commentary was based on the first event contributing to the composite outcome.

Table 5: Composite cardiovascular event with finerenone and placebo

Outcome	Finerenone n (%)	Placebo n (%)	HR (95% CI)
FIDELIO-DKD [key secondary outcome]			
Composite cardiovascular events	367/2,833 (13.0%)	420/2,841 (14.8%)	**0.86 (0.75, 0.99)**
- Cardiovascular death	98 (3.5%)	115 (4.0%)	-
- Non-fatal myocardial infarction	65 (2.3%)	82 (2.9%)	-
- Non-fatal stroke	81 (2.9%)	80 (2.8%)	-
- Hospitalisation for heart failure	124 (4.4%)	146 (5.1%)	-
FIGARO-DKD [primary outcome]			
Composite cardiovascular events	458/3,686 (12.4%)	519/3,666 (14.2%)	**0.87 (0.76, 0.98)**
- Cardiovascular death	147 (4.0%)	174 (4.7%)	-
- Non-fatal myocardial infarction	101 (2.7%)	93 (2.5%)	-
- Non-fatal stroke	100 (2.7%)	103 (2.8%)	-
- Hospitalisation for heart failure	110 (3.0%)	152 (4.1%)	

Source: Table 36 (p59) of the submission; Table 14.2.2.1/2 (p8) of the FIDELIO-DKD trial report; Table 14.2.1/2 (p5) of the FIGARO-DKD trial report

Abbreviations: CI, confidence interval; HR, hazard ratio

Note: For each subject only the first occurrence of a component of the composite efficacy outcome event is considered. If a subject experienced 2 or more events on the same date, all these events are presented.

Note: Bolding indicates a statistically significant difference

6.13 Treatment with finerenone was associated with a statistically significant reduction in the composite risk of cardiovascular events compared to placebo. This difference was primarily driven by a reduction in patients experiencing hospitalisation for heart failure as well as a reduction in cardiovascular death.

6.14 Composite renal events (including $\geq$ 40% decrease in eGFR) reported with finerenone and placebo treatment in the FIDELIO-DKD and FIGARO-DKD trials are summarised in Table 6 below. This was the primary outcome of the FIDELIO-DKD trial and a key secondary outcome of the FIGARO-DKD trial. The incidence of component outcomes reported in the commentary was based on the first event contributing to the composite outcome.

Table 6: Composite renal events (including ≥ 40% decrease in eGFR) with finerenone and placebo

Outcome	Finerenone n (%)	Placebo n (%)	HR (95% CI)
FIDELIO-DKD [primary outcome]			
Composite renal events	504/2,833 (17.8%)	600/2,841 (21.1%)	**0.83 (0.73, 0.93)**
- Renal failure	89 (3.1%)	82 (2.9%)	-
- Sustained ≥ 40% relative decrease in eGFR from baseline	477 (16.8%)	571 (20.1%)	
- Renal death	0 (0%)	1 (<0.1%)	
FIGARO-DKD [key secondary outcome]			
Composite renal events	350/3,686 (9.5%)	395/3,666 (10.8%)	0.87 (0.76, 1.01)
- Renal failure	17 (0.5%)	18 (0.5%)	
- Sustained ≥ 40% relative decrease in eGFR from baseline	338 (9.2%)	385 (10.5%)	
- Renal death	0 (0%)	0 (0%)	

Source: Table 37 (p60) of the submission; Table 14.2.1/2 (p5) of the FIDELIO-DKD trial report; Table 14.2.2.1/2 (p10) of the FIGARO-DKD trial report

Abbreviations: CI, confidence interval; HR, hazard ratio; NR, not reported

Note: For each subject only the first occurrence of a component of the composite efficacy outcome event is considered. If a subject experienced 2 or more events on the same date, all these events are presented.

Note: Bolding indicates a statistically significant difference

6.15 Treatment with finerenone was associated with a statistically significant reduction in the composite risk of renal events compared to placebo in the FIDELIO-DKD trial. This difference was primarily driven by a reduction in patients experiencing a sustained ≥ 40% relative decrease in eGFR from baseline. A similar pattern of results was also observed in the FIGARO-DKD trial, although the difference between treatment arms was not statistically significant.

6.16 The key composite outcomes and individual clinical outcomes from the FIDELITY pooled analysis of individual patient data are summarised in Table 7 below.

Table 7: Clinical outcomes with finerenone and placebo from the FIDELITY pooled analysis

Outcome	Finerenone N = 6,519 n (%)	Placebo N = 6,507 n (%)	HR (95% CI)
Key composite outcomes			
Time to first cardiovascular event[a]	825 (12.7%)	939 (14.4%)	**0.86 (0.78, 0.95)**
Time to first renal event (including ≥ 40% decrease in eGFR)[b]	854 (13.1%)	995 (15.3%)	**0.85 (0.77, 0.93)**
Time to first renal event (including ≥ 57% decrease in eGFR)[c]	360 (5.5%)	465 (7.1%)	**0.77 (0.67, 0.88)**
Time to all-cause mortality	552 (8.5%)	614 (9.4%)	0.89 (0.79, 1.00)
Time to all-cause hospitalisation	2,836 (43.5%)	2,926 (45.0%)	0.96 (0.91, 1.01)
Individual clinical outcomes			
Time to onset of kidney failure	254 (3.9%)	297 (4.6%)	**0.84 (0.71, 0.99)**
Time to sustained ≥ 40% relative decrease in eGFR from baseline	817 (12.5%)	962 (14.8%)	**0.84 (0.76, 0.92)**
Time to sustained ≥ 57% relative decrease in eGFR from baseline	257 (3.9%)	361 (5.5%)	**0.70 (0.60, 0.83)**
Time to renal death	2 (<0.1%)	4 (<0.1%)	0.53 (0.10, 2.91)
Time to first non-fatal stroke	198 (3.0%)	198 (3.0%)	0.99 (0.82, 1.21)
Time to first non-fatal myocardial infarction	173 (2.7%)	189 (2.9%)	0.91 (0.74, 1.12)
Time to first heart failure hospitalisation	256 (3.9%)	325 (5.0%)	**0.78 (0.66, 0.92)**
Time to cardiovascular death	322 (4.9%)	364 (5.6%)	0.88 (0.76, 1.02)
Time to non-cardiovascular, non-renal death	228 (3.5%)	246 (3.8%)	0.92 (0.77, 1.10)
Time to first cardiovascular hospitalisation	1,208 (18.5%)	1,279 (19.7%)	0.93 (0.86, 1.00)
Time to first non-cardiovascular hospitalisation	2,272 (34.9%)	2,301 (35.4%)	0.98 (0.93, 1.04)

Source: Table 44 (p68), Table 45 (p69), Table 46 (p71), Table 47 (p72), Table 60 (p110), Table 64 (p114) of the submission; Table 14.2.2/1 (p4), Table 14.2.2/3 (p6), Table 14.2.1/1 (p5), Table 14.2.1/3 (p9), Table 14.2.3/19 (p34), Table 14.2.3/21 (p36) of the FIDELITY pooled analysis

Abbreviations: CI, confidence interval; HR, hazard ratio; NR, not reported

Note: Bolding indicates a statistically significant difference

[a] Composite of the time to cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or hospitalisation due to heart failure

[b] Composite of the time to kidney failure, sustained decrease of eGFR greater or equal to 40% from baseline over at least 4 weeks, or renal death

[c] Composite of the time to kidney failure, sustained decrease of eGFR greater or equal to 57% from baseline over at least 4 weeks, or renal death

6.17 Treatment with finerenone was associated with a statistically significant reduction in cardiovascular and renal (using either the 40% or 57% eGFR threshold) composite outcomes compared to placebo. Exploratory analyses of individual outcomes suggested that treatment with finerenone was associated with reductions in heart failure hospitalisation, worsening renal impairment and progression to kidney failure.

6.18 Further exploratory analyses of cardiovascular mortality indicate that, while finerenone was not associated with a statistically significant reduction in the broader category of cardiovascular death, it may be associated with a reduction in sudden cardiac death and death due to heart failure. However, further analyses of myocardial infarction and stroke exploratory outcomes did not clearly demonstrate a reduction in risk with finerenone treatment.

6.19 The pre-specified subgroup analyses of cardiovascular outcomes did not suggest any major treatment effect interactions (see Table 8 and Table 9). The ESC considered that the impact of the interaction between finerenone and SGLT2 inhibitors and GLP-1 analogues on overall outcomes was unclear, although noted that the post hoc

subgroup analyses suggested that the benefits of finerenone were maintained with or without concomitant use of these medications. The PBAC noted the discordant effects across the 2 key trials and the imprecision of the post hoc subgroup analyses, resulting in wide confidence intervals, limited reliable interpretation of the results.

6.20 The PBAC also noted the ongoing CONFIDENCE trial (NCT05254002) investigating finerenone versus empagliflozin versus combination therapy and considered that this trial design could only be ethically justified if there was equipoise regarding the additive benefit of finerenone to an SGLT2 inhibitor.

Table 8: Key subgroup analyses of the cardiovascular composite endpoint from FIDELIO-DKD, FIGARO-DKD and FIDELITY

Subgroup	FIDELIO-DKD, n/N (rate per 100 patient years)				FIGARO-DKD, n/N (rate per 100 patient years)				FIDELITY, n/N (rate per 100 patient years)			
	FIN	PBO	HR (95% CI)	Interaction p-value	FIN	PBO	HR (95% CI)	Interaction p-value	FIN	PBO	HR (95% CI)	Interaction p-value
Baseline UACR mg/g												
< 30	0/11 (0.0)	2/12 (5.53)	NC		10/109 (2.64)	13/98 (4.13)	0.67 (0.27, 1.66)		10/120 (2.43)	15/110 (4.27)	0.59 (0.24, 1.45)	
30 to < 300	34/350 (3.33)	41/335 (4.25)	0.76 (0.48, 1.20)	NC	226/1,726 (3.88)	251/1,688 (4.42)	0.87 (0.73, 1.04)	0.6023	260/2,076 (3.79)	292/2,023 (4.40)	0.86 (0.73, 1.02)	0.4104
≥ 300	332/2,470 (5.42)	377/2,493 (6.19)	0.87 (0.75, 1.01)		222/1,851 (3.94)	254/1,878 (4.49)	0.90 (0.75, 1.08)		554/4,321 (4.71)	631/4,371 (5.37)	0.89 (0.79, 1.00)	
SGLT2 inhibitor use at baseline												
No	352/2,709 (5.12)	405/2,706 (5.99)	0.85 (0.74, 0.98)	0.4553	434/3,372 (4.01)	482/3,362 (4.50)	0.89 (0.78, 1.01)	0.1141	786/6,081 (4.44)	887/6,068 (5.08)	0.87 (0.79, 0.96)	0.4052
Yes	15/124 (4.90)	15/135 (4.44)	1.12 (0.55, 2.30)		24/314 (2.37)	37/304 (3.95)	0.49 (0.28, 0.86)		39/438 (2.95)	52/439 (4.08)	0.63 (0.40, 1.00)	

Source: Figure 9-23 (p 139), Figure 9-24 (p 140-141), Figure 14.2.4/12 (p 728-730) of the FIDELIO-DKD trial report; Figure 9-25 (p 145), Figure 9-26 (p 146-148) of the FIGARO-DKD trial report; Table 14.2.6.1/1 (p 31-38) of the FIDELITY pooled analysis
Abbreviations: NC, not calculable

Table 9: Key subgroup analyses of the renal composite endpoint from FIDELIO-DKD, FIGARO-DKD and FIDELITY

Subgroup	FIDELIO-DKD, n/N (rate per 100 patient years)				FIGARO-DKD, n/N (rate per 100 patient years)				FIDELITY, n/N (rate per 100 patient years)			
	FIN	PBO	HR (95% CI)	Interaction p-value	FIN	PBO	HR (95% CI)	Interaction p-value	FIN	PBO	HR (95% CI)	Interaction p-value
Baseline UACR mg/g												
< 30	0/11 (0.0)	2/12 (7.3)	NC		4/109 (1.11)	3/98 (0.99)	0.58 (0.09, 3.57)		4/120 (1.02)	5/110 (1.52)	0.58 (0.09, 3.57)	
30 to < 300	19/350 (1.90)	20/335 (2.11)	0.92 (0.49, 1.72)	NC	145/1,726 (2.63)	124/1,688 (2.30)	1.16 (0.91, 1.47)	**0.0188**	164/2,076 (2.52)	144/2,023 (2.27)	1.11 (0.88, 1.39)	**0.0322**
≥ 300	485/2,470 (8.65)	578/2,493 (10.26)	0.83 (0.73, 0.93)		201/1,851 (3.83)	268/1,878 (5.02)	0.74 (0.62, 0.90)		686/4,321 (6.32)	846/4,371 (7.71)	0.81 (0.73, 0.89)	

Subgroup	FIDELIO-DKD, n/N (rate per 100 patient years)				FIGARO-DKD, n/N (rate per 100 patient years)				FIDELITY, n/N (rate per 100 patient years)			
	FIN	PBO	HR (95% CI)	Interaction p-value	FIN	PBO	HR (95% CI)	Interaction p-value	FIN	PBO	HR (95% CI)	Interaction p-value
SGLT2 inhibitor use at baseline												
No	490/2,709 (7.73)	590/2,706 (9.39)	0.82 (0.72, 0.92)	0.2114	328/3,372 (3.23)	371/3,362 (3.65)	0.88 (0.76, 1.03)	0.6875	818/6,081 (4.96)	961/6,068 (5.85)	0.84 (0.77, 0.93)	0.5971
Yes	14/124 (4.66)	10/135 (3.07)	1.38 (0.61, 3.10)		22/314 (2.30)	24/304 (2.68)	0.70 (0.37, 1.30)		36/438 (2.87)	34/439 (2.79)	0.71 (0.42, 1.20)	

Source: Figure 9-21 (p 136), Figure 9-22 (p 137-138) of the FIDELIO-DKD trial report; Figure 9-27 (p 150); Figure 14.2.4/12 (p 732-734) of the FIGARO-DKD trial report; Figure 14.2.6.1/9 (p 40-46) of the FIDELITY pooled analysis 'bay948862_ia_fidelio_figaro_section_14_2_6_1'
Abbreviations: NC, not calculable; NR, not reported

6.21 The pre-specified subgroup analyses of renal outcomes strongly suggested that baseline BMI was a treatment effect modifier (BMI < 30 kg/m^2: HR 0.71 95% CI 0.62, 0.82; BMI ≥ 30 kg/m^2: HR 0.99 95% CI 0.88, 1.13; interaction term: p=0.0004). The subgroup analyses also suggested treatment effect interactions by region (larger treatment effects in Asian region), race (larger treatment effects in Asian populations), albuminuria (larger treatment effects in patients with higher albuminuria) and baseline potassium (smaller treatment effects in patients with higher potassium levels). The PBAC particularly noted the baseline albuminuria subgroup analyses for the renal endpoint: UACR < 30 mg/g: HR 0.58 95% CI 0.09, 3.57; UACR 30 to < 300 mg/g: HR 1.11 95% CI 0.88, 1.39; UACR ≥ 300 mg/g: HR 0.81 (0.73, 0.89): interaction term: p=0.0322).

6.22 Treatment with finerenone was associated with an initial reduction in eGFR compared to placebo in the first 4 months of treatment but was then associated with a slower decline over time. Treatment with finerenone was also associated with a rapid improvement in urinary albumin-to-creatinine ratio in the first 4 months of treatment that appeared to be maintained over time.

6.23 There were no major differences in quality of life scores (EQ-5D-5L and Kidney Disease Quality of Life, KDQOL-36) between finerenone and placebo treatment arms.

Comparative harms

6.24 Key safety outcomes with finerenone and placebo from the FIDELITY pooled analysis of individual patient data are summarised in Table 10.

Table 10: Safety outcomes with finerenone and placebo from the FIDELITY pooled analysis

Outcome	Finerenone N = 6,510 n (%)	Placebo N = 6,489 n (%)	OR (95% CI)
Any adverse event	5,602 (86.1%)	5,607 (86.4%)	0.97 (0.88, 1.07)
Treatment-related adverse event	1,206 (18.5%)	862 (13.3%)	**1.48 (1.35, 1.63)**
Serious adverse event	2,060 (31.6%)	2,186 (33.7%)	**0.91 (0.85, 0.98)**
Adverse events leading to discontinuation	414 (6.4%)	351 (5.4%)	**1.19 (1.03, 1.38)**
Adverse events leading to death	110 (1.7%)	151 (2.3%)	NR
Adverse events of interest			
Hyperkalaemia	912 (14.0%)	448 (6.9%)	**HR: 1.91 (1.72, 2.12)**
Hyperkalaemia leading to hospitalisation	61 (0.9%)	10 (0.2%)	**HR: 2.93 (1.90, 4.54)**
Acute kidney injury	220 (3.4%)	234 (3.6%)	NR
Decreased glomerular filtration rate	348 (5.3%)	274 (4.2%)	NR

Source: Table 48 (p73), Table 50 (p75), Table 71 (p117) of the submission; Table 3, Agarwal et al 2022 (p8)
Abbreviations: CI, confidence interval; HR, hazard ratio NR, not reported; OR, odds ratio
Note: Bolding indicates a statistically significant difference

6.25 Treatment with finerenone was associated with an increased incidence of treatment-related adverse events and adverse events leading to discontinuation compared to placebo. Adverse events occurring more frequently in the finerenone arm included hyperkalaemia, decreased glomerular filtration rate, hypotension, hyperuricaemia, pruritis and increased blood potassium. The increased risk of hyperkalaemia leading to hospitalisation with finerenone treatment occurred despite careful selection of the patient population, intensive monitoring and dose adjustments (down-titrations and dose interruptions) as well as increased use of potassium lowering agents.

6.26 Finerenone treatment was associated with a decreased incidence of serious adverse events compared to placebo primarily due to a reduction in pneumonia and complications associated with underlying diabetic kidney disease.

Benefits/harms

6.27 Based on the FIDELITY analysis, for every 1,000 patients treated with finerenone in comparison with placebo over 3 years:

- There would be 17 fewer cardiovascular events (primarily hospitalisation for heart failure).
- There would be 22 fewer renal events (primarily sustained worsening of kidney function).
- There would be 71 additional patients experiencing a hyperkalaemia event with 7 requiring hospitalisation.

6.28 The ESC noted that based on the FIGARO-DKD analysis (Pitt, 2021), the number needed to treat (NNT) is 47 (95% CI, 26 to 226) patients over 3.5 years to prevent a single cardiovascular event. Based on the FIDELIO-DKD analysis (Bakris, 2020), the NNT is 29 (95% CI, 16 to 166) patients over 3 years to prevent a single renal event and 42 (95% CI, 22 to 397) patients over 3 years to prevent a single cardiovascular event.

Clinical claim

6.29 The submission described finerenone plus standard of care as superior in terms of efficacy and comparable in terms of safety compared to placebo plus standard of care. The ESC considered that this claim was reasonable in the context of the clinical trials, although based on the NNT analyses noted above, the added benefit of finerenone is modest. Furthermore, the trial data was of uncertain applicability to Australian clinical practice, particularly in the context of a rapidly evolving treatment landscape.

6.30 The PBAC considered that a claim of modestly superior comparative efficacy was reasonable for the duration of the trials in the broader trial populations but was concerned that the subgroup analyses suggested little to no treatment benefit in patients with less than very high albuminuria at baseline. It further noted that the size of the comparative gain in patients treated with an SGLT2 inhibitor was highly uncertain.

6.31 The PBAC considered that a claim of comparable safety was not adequately supported by the data, given that the reduction in serious adverse events was partly driven by a reduction in complications associated with diabetic kidney disease, and that the risk of hyperkalaemia was likely to be greater outside the tightly controlled environment of a clinical trial.

Economic analysis

6.32 The submission presented a stepped economic evaluation of finerenone plus standard of care compared to placebo plus standard of care for the treatment of diabetic kidney disease. The economic evaluation was based on the pooled FIDELITY analysis with additional modelled data. The economic evaluation was presented as a cost-effectiveness/cost-utility analysis.

6.33 The economic analysis did not capture the costs, benefits and harms of finerenone displacing existing MRAs for patients with comorbid conditions such as heart failure and treatment-resistant essential hypertension. However, the ESC advised that the restriction should explicitly exclude patients on other MRAs or patients with established HFrEF and an indication for an MRA, which would prevent switching between these agents.

Table 11: Key components of the economic evaluation

Component	Description
Type of analysis	Cost-effectiveness/cost-utility analysis
Outcomes	Patients free of renal failure and/or cardiovascular events; quality adjusted life years
Time horizon	15 years in the model base case versus 3 years in the clinical trials
Methods used to generate results	Markov state-transition cohort model
Treatments	Finerenone; placebo
Health states	24 health states based on severity of kidney disease (CKD 1/2, CKD 3, CKD 4, CKD 5, acute/chronic dialysis, acute/chronic transplantation), the presence or absence of an acute cardiovascular event and the presence or absence of a history of cardiovascular events. The model also included 2 death states; cardiovascular death and background mortality.
Cycle length	4 months with half-cycle corrections
Patient characteristics and circumstances of use	Mean age, gender and baseline distribution across CKD stages was estimated based on the pooled FIDELITY patient population. The model assumed that patients had no prior history of cardiovascular events. The submission assumed perfect adherence to treatment until discontinuation, with treatment persistence estimates based on the pooled FIDELITY analysis. The model did not explicitly capture finerenone dose titrations. The use of background therapies was estimated based on the baseline use of medications from the pooled FIDELITY analysis.
Transition probabilities	Placebo health state transitions and event risks were based on individual patient data from the pooled FIDELITY analysis. The risk of cardiovascular death was also based on the pooled FIDELITY analysis. The risk of background mortality was based on Australian life tables adjusted to exclude cardiovascular and renal causes of death with additional mortality multipliers applied from the published literature (Darlington 2021, Erickson 2013, 22nd Annual UK Renal Registry data report). Finerenone treatment effects (time to dialysis, time to CKD 5 without dialysis/transplantation, first non-fatal cardiovascular event, cardiovascular death, subsequent cardiovascular events, hyperkalaemia with or without hospitalisation) were estimated based on pre-specified and post hoc analyses of the pooled FIDELITY data with additional assumptions. Treatment effects were assumed to remain constant over time while on treatment. The risk of treatment discontinuation was also based on the pooled FIDELITY analysis assuming that the rate of discontinuation remains constant over time. Patients discontinuing finerenone treatment were assumed to have the same risk as placebo patients.
Utility values	All utility/disutility values were derived from a post hoc analysis of EQ-5D-5L utility data from the pooled FIDELITY analysis. Utility data were collected at scheduled visits (on an annual basis) and at treatment/study discontinuation using the EQ-5D-5L instrument with UK tariffs. The submission mapped the visit data to health states and events by identifying utility values reported within 4 months of an event (acute), reported after an event but not within 4 months (chronic) or reported after an event at any time. The utility data were analysed based on a multilevel repeated measurement model using a generalised estimating equation with various demographic and disease characteristics as covariates.

Component	Description
Costs	Finerenone drugs costs were estimated based on the proposed price. Background therapy costs were estimated based on the utilisation of different drug classes in the pooled FIDELITY analysis with costs estimated for a representative member of each drug class using published PBS prices. The costs of hyperkalaemia without hospitalisation were based on MBS costs assuming that patients would require a specialist visit and a serum potassium test. The cost of hyperkalaemia with hospitalisation was based on AR-DRG cost weights. The costs of acute non-fatal myocardial infarction and heart failure were based on AR-DRG cost weights. The submission assumed no chronic costs for myocardial infarction or heart failure patients. The costs of acute/chronic non-fatal stroke were based on published estimates from an Australian stroke study (Cadilhac 2009). The costs of CKD health states (CKD 1/2, 3, 4, 5) were based on published estimates for diabetic kidney disease from an Australian costing study (Wyld 2015). The costs of acute/chronic dialysis were estimated based on previously published data from NSW Health (NSW Dialysis Costing Studies, 2009) with additional costs for initial access based on AR-DRG costs weights. The costs of transplantation were estimated from a modelled economic analysis of diabetes, hypertension, and chronic kidney disease management in Australia (Howard 2010) and a published comparative modelled analysis of dialysis and transplantation in Australia (Wong 2012). The cost of cardiovascular death was assumed to be the same as a non-fatal cardiovascular event. The submission assumed no costs associated with background mortality. Costs estimated in the submission were inflated to 2021 values using the health sub-category of the consumer price index (CPI). The ESC considered it unclear why the submission had not used more recent AR-DRG costs where available rather than relying on large inflation factors.
Discount rate	5% for costs and outcomes
Software package	Microsoft Excel

Source: Table 56 (pp89-91); Section 3.2-3.6 (pp93-133) of the submission
Abbreviations: AR-DRG, Australian Refined Diagnosis Related Groups; CKD, chronic kidney disease; CPI, consumer price index; MBS, Medicare Benefit Schedule

6.34 All patients began the model with various levels of renal impairment (CKD 1/2, CKD 3, CKD 4) with the assumption of no prior history of cardiovascular events. During each cycle of the Markov model, patients could remain in their current health state, experience progression/regression of renal impairment, initiate dialysis or transplantation, experience an acute non-fatal cardiovascular event, or die from cardiovascular or background mortality. Patients experiencing an acute non-fatal cardiovascular event or initiating dialysis/transplantation transition to a corresponding chronic disease state in the next cycle. Patients in both treatment arms could also experience hyperkalaemia events with or without hospitalisation in any cycle. Patients in the finerenone arm could discontinue treatment in any cycle and adopt the same risks as the placebo arm.

6.35 The submission estimated finerenone treatment effects based on aggregate-level data from the FIDELITY pooled analysis. The submission stated that key cardiovascular and renal outcomes from the FIDELITY analysis were not used in the economic model as composite outcomes are difficult to incorporate into an economic evaluation given that each component has a different impact on costs, utilities and risk of future events.

Instead, the submission used various pre-specified and post hoc exploratory analyses to populate the economic model (summarised in Table 12).

6.36 Treatment effects were applied to placebo arm transition probabilities to derive transition probabilities for the finerenone arm. The application of a decreased risk of CKD progression in the finerenone arm resulted in a series of adjustments that increased the probabilities of both disease stabilisation and disease regression for this treatment arm. The ESC noted that, with the exception of the progression to CKD 5 without dialysis or transplantation, all treatment effects included in economic model were not statistically significant.

Table 12: Finerenone treatment effects included in the model

Variable	Hazard ratio (95% CI)	Source
Progression to CKD 5 without dialysis or transplantation	**0.81 (0.67, 0.98)**	Pre-specified analysis of the time to a sustained decrease in eGFR to < 15 mL/min from the pooled FIDELITY data which included patients with and without progression to dialysis/transplantation
Progression to dialysis	0.82 (0.65, 1.03)	Post hoc analysis of the pooled FIDELITY data which included patients with and without a sustained decrease in eGFR to < 15 mL/min
Progression to kidney transplant	1.00	Assumption (no justification stated)
First non-fatal cardiovascular event	0.88 (0.76, 1.03)	Post hoc analysis of the pooled FIDELITY data which was a composite outcome consisting of non-fatal myocardial infarction, non-fatal stroke and non-fatal heart failure
Subsequent cardiovascular event	0.84 (0.68, 1.05)	Post hoc analysis of the pooled FIDELITY data which was a composite outcome consisting of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke and non-fatal heart failure
Cardiovascular death	0.88 (0.76, 1.02)	Pre-specified analysis of the pooled FIDELITY data which includes both first and subsequent cardiovascular events
Hyperkalaemia without hospitalisation	1.91 (1.72, 2.12)	Post hoc analysis of the pooled FIDELITY data
Hyperkalaemia with hospitalisation	2.93 (1.90, 4.54)	Post hoc analysis of the pooled FIDELITY data

Source: Table 60 (p110), Table 64 (p114), Table 66 (p114), Table 71 (p117) of the submission
Note: Bolding indicates a statistically significant difference

6.37 Key drivers of the economic model are summarised in Table 13.

Table 13: Key drivers of the model

Description	Method/Value	Impact
Baseline risk	The baseline risk for the majority of modelled events (with the exception of background mortality) was derived from individual patient data for placebo patients in the pooled FIDELITY analysis. The submission did not adequately address how the use of quota-sampling, limited use of SGLT2 inhibitors/GLP1 analogues, exclusion of mineralocorticoid receptor antagonists and intensive hyperkalaemia management in the clinical trials would affect the underlying risk of events compared to the proposed target population. The allocation of patients to baseline health states assumed that patients had no prior history of cardiovascular events which was inconsistent with the clinical data from the FIDELITY pooled analysis which indicated that 45.6% of trial participants had a prior history of cardiovascular events. The impact of the misallocation of patients to baseline	High, favours finerenone

Description	Method/Value	Impact
	health states was unclear. The submission assumed that the proportions of patients using conservative care (CKD 5), dialysis or transplantation for kidney failure in the clinical trials would be representative of the Australian setting. However, use of these therapies in clinical practice is highly dependent on local circumstances in each healthcare setting and the submission did not provide any data to support the applicability of these estimates. The ESC agreed with the evaluation that the trial data had a number of applicability issues (discussed in more detail under 'Clinical trials'). The ESC advised that the baseline risk in the economic model should be adjusted for subgroups of patients with and without high albuminuria, prior cardiovascular disease, and concomitant SGLT2 inhibitor use. The pre-PBAC response provided a sensitivity analysis for CKD severity, which applied the OneNil dataset baseline CKD stage distribution (CKD 1/2: 56.3%; CKD 3: 39.6%; CKD 4: 4.1%) rather than the FIDELITY pooled analysis (CKD 1/2: 39.9%; CKD 3: 53.3%; CKD 4: 6.8%) increasing the 'alternative base case' ICER from $55,000 to < $75,000 to $55,000 to < $75,000.	
Finerenone treatment effects	The submission estimated finerenone treatment effects based on various pre-specified and post hoc exploratory analyses using aggregate-level data from the FIDELITY pooled analysis. Treatment effects were applied to placebo arm transition probabilities to derive transition probabilities for the finerenone arm. The separate modelling of treatment effects for 'progression to CKD 5 without dialysis or transplantation' and 'progression to dialysis' implicitly assumed that these treatment effects are completely independent of each other. The evaluation considered that this assumption was not reasonable as a delay in the time to CKD progression with finerenone treatment would be expected to also delay dialysis, resulting in substantial overlap of estimated treatment effects. In the absence of any data demonstrating independent treatment effects (such as a delay in dialysis progression for patients already in CKD 5) it would be more appropriate to only include one of the renal treatment effects in the economic model. The PSCR argued that 'progression to CKD 5 without dialysis or transplantation' and 'progression to dialysis' was modelled separately in order to account for the finerenone treatment benefit of prolonged delay to dialysis despite progression to CKD 5 compared with placebo. The PSCR also stated that the annual probability of transitioning from 'CKD5 – without dialysis' to 'dialysis' in the clinical trials was 15.61% and 18.72% in the finerenone and placebo arms, respectively, which meant that the model structure reflected the trial evidence. The PSCR plotted the time to dialysis in the model versus the FIDELITY trial results (Figure 1, p6) to support its claim that progression to dialysis was consistent between the trial and economic evaluation. The time to event data for these transitions were not provided and therefore the estimates could not be validated. The ESC agreed with the evaluation that the separation of these treatment effects in the economic model was not appropriate and considered that once CKD 5 is reached, the decision to commence dialysis is often a patient decision or related to access and is unlikely to be influenced by finerenone use in practice. The pre-PBAC response maintained that the modelled finerenone treatment benefit of prolonged delay to dialysis was appropriate and considered its removal in the alternative base case highly conservative. The submission did not adequately justify the construction of new composite endpoints for first non-fatal cardiovascular event and subsequent cardiovascular event particularly given the acknowledged limitations of composite endpoints. Data on individual cardiovascular outcomes from the pooled FIDELITY analysis suggest a reduction in heart failure events with finerenone treatment but do not clearly support reductions in myocardial infarction and stroke events. Additionally, the estimation of a larger treatment effect for subsequent cardiovascular events compared to initial cardiovascular events	High, favours finerenone

Description	Method/Value	Impact
	was inconsistent with subgroup analyses which indicated that history of cardiovascular disease was not a treatment effect modifier for cardiovascular outcomes. The subgroup analyses of the finerenone trials strongly suggested that baseline BMI was a treatment effect modifier for renal events. The subgroup analyses also suggested treatment effect interactions by region, race, albuminuria and baseline potassium levels. Differences in any of these characteristics between the trial populations and the proposed PBS population are likely to affect the modelled effectiveness of finerenone treatment. The assumption that treatment effects are maintained while on treatment was not adequately supported for the modelled outcomes of progression to dialysis, progression to CKD 5 without dialysis/transplantation, cardiovascular death, first non-fatal cardiovascular event, subsequent cardiovascular event and hyperkalaemia events.	
Dialysis health state costs	The submission estimated the costs for dialysis health states based on the 2009 NSW Dialysis Costing Study. The submission also included an additional cost for dialysis access surgery based on unspecified AR-DRG cost weights reported in a modelled economic analysis of diabetes, hypertension, and chronic kidney disease management in Australia (Howard 2010). The submission also included an additional cost for disease management based on chronic kidney disease estimates (CKD 3, 4, 5) from the Wyld 2015 publication. Dialysis costs were inflated to 2021 values using the health sub-category of the consumer price index. Total estimated costs were $[redacted] in first cycle and $[redacted] in subsequent cycles, which the ESC considered to be implausibly high for a 4-month cycle. The inflation of costs using the CPI index (measures inflation to households) was inadequately justified. The PBAC Guidelines v5.0 recommend the use of the AIHW health inflation index, which measures inflation across the health sector, to adjust costs over time. The PSCR used AIHW inflation factors to adjust cost inputs in the model, which increased the ICER to $25,000 to < $35,000 per QALY gained, compared with $5,000 to < $15,000 per QALY gained in the base case. The evaluation considered inclusion of additional costs for dialysis surgery was inappropriate as these costs were already captured in the dialysis treatment costs reported in the NSW Health study. The ESC noted the PSCR suggestion that that the likelihood of double counting surgery costs was low because the NSW Health survey reported pre-dialysis admitted hospital costs to be 'partially in scope' of the study, with acute expenditures presented independently of dialysis costs by modality, and given data was cross-sectional the initial costs would be diluted. However, the ESC considered the risk of double counting remained and not including this additional cost was more appropriate. During the evaluation, alternative dialysis health state costs were estimated by using the AIHW health inflation index and removing the cost of dialysis access surgery which resulted in substantially lower costs for dialysis. Total estimated costs were $[redacted] in first and subsequent cycles, and the resulting ICER was $25,000 to < $35,000 per QALY gained. The ESC advised that the cost for dialysis estimated by the evaluation more accurately reflected current Australian medical costs than that estimated in the submission.	High, favours finerenone
Model structure	The structure of the economic model was largely built around renal impairment/kidney failure health states with the exception of 3 modelled variables: subsequent cardiovascular events, hyperkalaemia events and treatment discontinuations. The decision not to link hyperkalaemia events and treatment discontinuations with renal impairment/kidney failure health states prevented an important interaction between these variables. Based on the natural history of chronic kidney disease it would be expected that as renal disease progresses, it becomes more difficult to maintain electrolyte	High, favours finerenone

Description	Method/Value	Impact
	balances and therefore events such as hyperkalaemia become more frequent and it becomes more difficult for a patient to remain on therapy with a potassium-sparing diuretic. This pattern appears to be consistent with data from the FIDELITY pooled analyses which indicated that both hyperkalaemia events and discontinuations were more frequent in patients with lower renal function. The PSCR argued that as most patients in the FIDELITY trial had poor renal function at baseline (approximately 60% with CKD 3 or worse), the unadjusted trial data adequately captured the risk of hyperkalaemia and risk of treatment discontinuation in these patients. The ESC noted that trial-based treatment compliance and hyperkalaemia events may not reflect treatment experience in the extrapolated period as disease progresses. The pre-PBAC response argued that subgroup analysis of the FIDELITY data showed no difference in the relative risk of hyperkalaemia by eGFR stage and therefore the linking of hyperkalaemia events and treatment discontinuations with renal impairment/kidney failure health states would have minimal impact on the results and would over complicate the model.	

Source: Constructed during the evaluation
Abbreviations: AIHW, Australian Institute of Health and Welfare; AR-DRG, Australian Refined Diagnosis Related Groups; CKD, chronic kidney disease; CPI, consumer price index; eGFR, estimated glomerular filtration rate; PBAC, Pharmaceutical Benefits Advisory Committee; PBS, Pharmaceutical Benefits Scheme

6.38 Although not a key driver of the model, the ESC considered the utility values of the health states to be high compared to other reported literature values and in some cases considered the relativities between the trial-based utilities to be implausible. For example, the CKD 1/2 health state was associated with a utility value of 0.782, which represents a health state that is predominately asymptomatic for many patients. However, the chronic transplant health state was associated with a utility of 0.885, despite the health and quality of life implications associated with transplant, such as immunosuppression and its adverse effects and fear of graft loss and return to dialysis. The ESC considered the utility values lacked face validity and advised they be replaced by values obtained from the literature.

6.39 The results of the stepped economic evaluation are summarised in Table 14 below.

Table 14: Stepped economic evaluation of finerenone compared to placebo for the treatment of diabetic kidney disease

Type of resource item	Finerenone	Placebo	Incremental difference
Step 1: Trial-based analysis (3 years) using finerenone drug costs only with no discounting, discontinuations, or mortality			
Costs	$	$0	$
Patients with renal failure	0.030	0.036	-0.006
Number of cardiovascular events	0.095	0.116	-0.021
Incremental cost per patient free of renal failure			$[1]
Incremental cost per cardiovascular event avoided			$[2]
Step 2a: Model-based analysis (3 years) with finerenone treatment effects applied to renal and hyperkalaemia outcomes; health state and event utility values included; treatment discontinuations included; finerenone drug costs only; discounting applied			
Costs	$	$0	$
QALYs	2.0721	2.0715	0.0007
Incremental cost per QALY gained			$[3]
Step 2b: Model-based analysis (3 years) with finerenone treatment effects applied to cardiovascular and hyperkalaemia outcomes; health state and event utility values included; treatment discontinuations included; finerenone drug costs only; discounting applied			
Costs	$	$0	$
QALYs	2.0776	2.0715	0.0061
Incremental cost per QALY gained			$[4]
Step 2c: Model-based analysis (3 years) with finerenone treatment effects applied to renal, cardiovascular and hyperkalaemia outcomes; health state and event utility values included; treatment discontinuations included; finerenone drug costs only; discounting applied			
Costs	$	$0	$
QALYs	2.0783	2.0715	0.0068
Incremental cost per QALY gained			$[4]
Step 3: Model-based analysis (3 years) with finerenone treatment effects applied to renal, cardiovascular and hyperkalaemia outcomes; health state and event utility values included; treatment discontinuations included; drug costs, event costs and health state costs included; discounting applied			
Costs	$	$29,095	$
QALYs	2.0783	2.0715	0.0068
Incremental cost per QALY gained			$[5]
Step 4: Model-based analysis (15 years) with finerenone treatment effects applied to renal, cardiovascular and hyperkalaemia outcomes; health state and event utility values included; treatment discontinuations included; drug costs, event costs and health state costs included; discounting applied			
Costs	$	$121,913	$
QALYs	6.2549	6.1774	0.0775
Incremental cost per QALY gained			$[6]

Source: Table 87 (p137) of the submission
Abbreviations: QALY, quality-adjusted life year
The redacted values correspond to the following ranges:
[1] *$555,000 to < $655,000*
[2] *$155,000 to < $255,000*
[3] *> $1,055,000*
[4] *$355,000 to < $455,000*
[5] *$255,000 to < $355,000*
[6] *$5,000 to < $15,000*

6.40 The inclusion of cardiovascular treatment effects and the extrapolation of treatment benefits beyond the clinical trial data had the largest impact on the stepped economic evaluation. The difference in total cost between treatment arms was driven by

finerenone drug costs which were largely offset by reduced costs associated with dialysis. The ESC noted that finerenone may delay time to dialysis and so costs would be delayed rather than avoided. The difference in total quality adjusted life years between treatment arms was primarily driven by a modelled increase in patient survival due to a reduction in cardiovascular and non-cardiovascular death (which were not statistically significantly different between treatment arms in the trials).

6.41 Based on the economic model, treatment with finerenone was associated with an incremental cost per QALY gained of $5,000 to < $15,000 compared to placebo for the management of diabetic kidney disease. The ESC advised that the estimated cost-effectiveness of finerenone, which was primarily based on data from the FIDELITY pooled analysis, was unlikely to be representative of the cost-effectiveness of finerenone in Australian clinical practice. In particular, the economic evaluation could have been strengthened to address some of the key translation issues by providing cost-effectiveness estimates for subgroups of patients with and without very high albuminuria, patients with and without prior cardiovascular disease, as well as patients with and without concomitant SGLT2 use.

6.42 For every 1,000 patients treated with finerenone plus standard of care versus placebo plus standard of care and followed up for 15 years, the economic evaluation (with discounting) estimated that there would be:

- Additional finerenone drug costs of $[redacted] with additional disease management costs of $[redacted] (background medications, health state costs and adverse events).
- Decreased incidence of dialysis (14 fewer initiations), transplant (1 fewer transplant), non-fatal cardiovascular events (60 fewer events), fatal cardiovascular events (8 fewer deaths) and other deaths (4 fewer deaths).
- Increased incidence of hyperkalaemia without hospitalisation (189 events) and hyperkalaemia with hospitalisation (21 events).
- Decreased costs for dialysis ($[redacted]) transplantation ($[redacted]) and cardiovascular events ($[redacted]).

6.43 The results of the sensitivity analyses indicated that the model was most sensitive to a shorter time horizon, population characteristics (informing baseline risk), finerenone treatment effects (particularly for renal outcomes) and dialysis costs. The ESC noted that a shorter time horizon would not be adequate to capture the delay to CKD 5.

Table 15: Results of sensitivity analyses

Analyses	Incremental cost	Incremental QALY	ICER
Base case	**$**	**0.0775**	**$**[1]
Discount rate (base case: 5% for benefits and costs)			
3.5% discount rate	$	0.0876	$[1]
0% discount rate	$	0.1188	$[2]
Time horizon (base case: 15 years)			
5 years	$	0.0167	$[3]
10 years	$	0.0484	$[4]
30 years	$	0.1056	$[1]
Patient population (base case: mean age 64.8 years; CKD ½: 39.9%, CKD3: 53.3%, CKD4: 6.8%)			
Assume all patients in CKD 1/2 at baseline	$	0.0663	$[5]
Assume all patients in CKD 3 at baseline	$	0.0800	$[1]
Assume all patients in CKD 4 at baseline	-$	0.1226	Dominant
Decrease mean age to 60 years	-$	0.0774	Dominant
Increase mean age to 70 years	$	0.0734	$[6]
Finerenone treatment effects (base case: CKD 5 progression HR 0.81; dialysis progression HR 0.82; first non-fatal CV event HR 0.88; fatal CV event HR 0.88; subsequent CV event HR 0.84; hyperkalaemia without hospitalisation HR 1.91; hyperkalaemia with hospitalisation HR 2.93)			
Upper 95% CI for CKD 5 progression (0.98)	$	0.0622	$[7]
Lower 95% CI for CKD 5 progression (0.67)	-$	0.0905	Dominant
Upper 95% CI for dialysis progression (1.03)	$	0.0664	$[8]
Lower 95% CI for dialysis progression (0.65)	-$	0.0872	Dominant
Upper 95% CI for first non-fatal CV event (1.03)	$	0.0707	$[4]
Lower 95% CI for first non-fatal CV event (0.76)	$	0.0831	$[2]
Upper 95% CI for fatal CV event (1.02)	-$	0.0239	Dominant
Lower 95% CI for fatal CV event (0.76)	$	0.1240	$[1]
Upper 95% CI for subsequent CV event (1.05)	$	0.0771	$[1]
Lower 95% CI for subsequent CV event (0.68)	$	0.0777	$[1]
Upper 95% CI for hyperkalaemia without hospitalisation (2.12)	$	0.0774	$[1]
Lower 95% CI for hyperkalaemia without hospitalisation (1.72)	$	0.0775	$[1]
Upper 95% CI for hyperkalaemia with hospitalisation (4.54)	$	0.0775	$[1]
Lower 95% CI for hyperkalaemia with hospitalisation (1.90)	$	0.0775	$[1]
Remove CKD 5 treatment effect	$	0.0604	$[7]
Remove dialysis treatment effect	$	0.0679	$[7]
Remove all renal treatment effects	$	0.0504	$[9]
Remove all cardiovascular treatment effects	$	0.0264	$[4]
Costs (base case: background therapy costs: $ per day; CKD ½: $ per cycle; CKD3-5: $ per cycle; acute dialysis: $ per cycle; chronic dialysis: $ per cycle; acute transplant: $ per cycle; chronic transplant: $ per cycle; acute CV event: $ per cycle; chronic CV event: $ per cycle; hyperkalaemia without hospitalisation: $ per event; hyperkalaemia with hospitalisation: $ per event)			
Background therapy costs removed	$	0.0775	$[1]
Alternative estimation of dialysis costs using no access charges and AIHW health inflation index	$	0.0775	$[6]
Increase CKD/dialysis/transplant costs by 25%	-$	0.0775	Dominant
Decrease CKD/dialysis/transplant costs by 25%	$	0.0775	$[4]
Increase CV costs by 25%	$	0.0775	$[1]
Decrease CV costs by 25%	$	0.0775	$[1]
Increase hyperkalaemia costs by 50%	$	0.0775	$[1]
Decrease hyperkalaemia costs by 50%	$	0.0775	$[1]

Source: Table 93 (p141-144) of the submission

Abbreviations: AIHW, Australian Institute of Health and Welfare; CI, confidence interval; CKD, chronic kidney disease; CV, cardiovascular; HR, hazard ratio

The redacted values correspond to the following ranges:
[1] *$5,000 to < $15,000*
[2] *$0 to < $5,000*
[3] *$95,000 to < $115,000*
[4] *$15,000 to < $25,000*
[5] *$35,000 to < $45,000*
[6] *$25,000 to < $35,000*
[7] *$45,000 to < $55,000*
[8] *$55,000 to < $75,000*
[9] *$115,000 to < $135,000*

6.44 During the evaluation, a multivariate sensitivity analysis was conducted based on using only one renal outcome treatment effect for finerenone to avoid overlapping treatment effects (CKD effects were retained while dialysis effects were removed, as this was a more favourable scenario for finerenone) and alternative costing estimates for dialysis (AIHW health inflation index and no double counting of access costs). The multivariate analysis was further tested with additional sensitivity analyses exploring the impact of population characteristics.

Table 16: Multivariate sensitivity analyses

Analyses	Incremental cost	Incremental QALY	ICER
Original base case	**$**	**0.0775**	**$** [1]
Alternative base case (no dialysis access surgery costs, AIHW health inflation index for dialysis cost estimates; dialysis treatment effects removed)	$	0.0679	$ [2]
Patient population (base case: mean age 64.8 years; CKD ½: 39.9%, CKD3: 53.3%, CKD4: 6.8%; male: 69.8%)			
Assume all patients in CKD 1/2 at baseline	$	0.0604	$ [3]
Assume all patients in CKD 3 at baseline	$	0.0699	$ [2]
Assume all patients in CKD 4 at baseline	$	0.0963	$ [1]

Source: Calculated during the evaluation
Abbreviations: AIHW, Australian Institute of Health and Welfare; CI, confidence interval; CKD, chronic kidney disease; CV, cardiovascular; HR, hazard ratio
The redacted values correspond to the following ranges:
[1] *$5,000 to < $15,000*
[2] *$55,000 to < $75,000*
[3] *$75,000 to < $95,000*

6.45 The multivariate analyses indicated that the cost-effectiveness of finerenone at the proposed price could plausibly be around $55,000 to < $75,000 per QALY gained but could vary substantially based on differences in baseline risk. The ESC advised that the alternative base case calculated during the evaluation was a more reasonable estimate of cost-effectiveness of finerenone, but still included optimistic treatment effect assumptions given the use of non-significant pooled trial data and assumptions regarding ongoing treatment benefit. Furthermore, the reliability of the alternative base case was still limited by issues with clinical evidence applicability and utilities as previously discussed.

6.46 The pre-PBAC response considered the alternative base case developed during the evaluation conservative, however accepted the analysis for the purposes of decision making.

Drug cost/patient/year

6.47 The submission proposed a flat pricing structure for both dose strengths (10 mg and 20 mg) of finerenone. The estimated drug cost for finerenone per patient per year was $ (based on the proposed DPMQ per script $ / 28 days per script x 365 days per year).

6.48 A comparison of finerenone use between the trial setting, the economic model and the financial estimates is presented in Table 17.

Table 17: Calculation of drug cost per year

	FIDELITY pooled analysis	Economic model	Financial estimates
Finerenone script cost	-		$
Treatment adherence	91.7%[a]	100% (assumption)	91.7%[a]
Treatment persistence	66.1% at 4 years	$ 66.1% at 4 years	Not directly estimated, was assumed to modify uptake rates in prevalent population

Source: Table 72 (p118); Table 85 (p132); Section 4.1-4.2 (pp146-459) of the submission
[a] It was unclear whether the adherence estimate accounted for dose titrations and dose interruptions in the trials.

Estimated PBS usage & financial implications

6.49 This submission was not considered by DUSC.

6.50 The submission used an epidemiological approach to estimate the utilisation and financial impact of listing finerenone. Key inputs relied on in the financial estimates are summarised in Table 18.

Table 18: Key inputs for financial estimates

Parameter	Value applied and source	Comment
Australian population age ≥25 years	18.7 million in year 1 increasing to 20.3 million in year 6. ABS population – 3222.0 Series A (high assumptions of fertility, life expectancy and net overseas migration) (years 2023-2028)	The submission did not justify the use of higher population estimates from ABS series A rather than series B as included in the standardised Excel workbook available from the PBAC Guidelines v5.0 website.
CKD prevalence	5.3 to 44.5% (by age bands). Based on biomedical measures from urine and blood samples of 11,200 Australian adults and children who participated in the 2011-12 National Health Measures Survey (NHMS 2013). CKD was defined as a single measure of eGFR < 60 mL/min/1.73m^2 and a UACR ≥ 2.5 mg/mmol for males and ≥ 3.5 mg/mmol for females.	Eligible population estimates were based on the pool of prevalent CKD patients. The applicability of the NHMS data to current practice was limited by the relatively old dataset. The authors also note the analysis was based on single measures of eGFR/UACR and therefore may include temporary fluctuations due to conditions unrelated to CKD (e.g. acute kidney injury, infections).
CKD diagnosis rate	50 to 75%. Based on CKD diagnosis rates recommended by the PBAC when considering the dapagliflozin submission for CKD (Table 23, dapagliflozin Public Summary Document (PSD), September 2021 PBAC meeting).	The ESC considered that diagnosis rates in the broader CKD population are unlikely to be applicable to patients with diabetes who are diagnosed with CKD. The ESC considered that CKD diagnosis among patients with diabetes is likely to be higher compared to a non-diabetic CKD patient population.

Parameter	Value applied and source	Comment
CKD patients with serum potassium < 5 mmoL/L who have comorbid diabetes	73%. Based on a retrospective hospital-based cohort study of CKD patients admitted to a Victorian hospital between 2014 and 2018 who had an admission potassium value. There were 3,566 patients with diabetes documented as a comorbidity (32% of the whole cohort), of whom 72.7% had a serum potassium of < 5 mmoL/L on admission.	The study assessed potassium abnormalities in hospitalised patients with CKD, which is unlikely to be applicable to general practice. The estimation of patients meeting the serum potassium threshold was inappropriate as it did not account for the use of ACEi/ARB, which is likely to increase potassium levels.
Patients on ACEi/ARB	80%. Based on the proportion of patients with CKD who are stable on ACEi/ARB (80%) recommended by the PBAC when considering the dapagliflozin CKD submission (para 15.4, dapagliflozin PSD, September 2021 PBAC meeting). The submission assumed the same proportion would apply to diabetic kidney disease patients.	The ESC considered this to be a reasonable assumption.
CKD patients with diabetes who meet UACR and eGFR eligibility criteria	18%. Based on a sponsor-commissioned analysis of the OneNil electronic medical records, primarily from general practice with limited coverage of specialist clinics. The analysis attempted to identify a FIDELITY-like population based on patients with at least one medical record between January 2016 and December 2020 with specific rules to identify patients with diabetes, CKD and albuminuria. Of those identified with CKD, approximately 18% had diabetes with eGFR and UACR in line with the proposed restriction.	The applicability of the OneNil patient cohort to clinical practice may be limited. Prior validation exercises conducted with the OneNil database indicate the dataset overrepresents older individuals, females, people from Victoria, people from disadvantaged backgrounds, patients from regional areas, and patients with Type 2 diabetes, hypertension, cardiovascular disease, gastro-oesophageal reflux disease, depression and anxiety. There is also potential for double counting and data gaps as there is no linking of data between clinics. The identification of CKD may be inadequate as it was based on the most recent eGFR/UACR, therefore the analysis appears unable to differentiate between transient (e.g. due to infection) versus persistent albuminuria. The identification of diabetes was based on either coded diagnosis in their clinical file or more recent HbA1c measurement ≥ 6.5%. Sensitivity analyses using alternative definitions (using combinations of HbA1c, coded diagnosis and medications) suggest wide-ranging proportions of diabetic kidney disease within CKD. The analysis did not consider utilisation of ACEi/ARB or potassium levels, therefore the estimate used is not applicable to those meeting the eGFR/UACR criteria.
Uptake rate	[redacted]–[redacted]%. Assumption. The submission stated the estimates that are applied to the prevalent population account for increasing uptake of finerenone over time and patients discontinuing finerenone due to death or initiation of renal replacement therapy.	The ESC considered that the uptake rates were implausibly high given the evolving treatment landscape and the discontinuation rates in the pivotal trials (34% at 4 years in FIDELITY, 40% at 4 years in FIDELIO-DKD and 30% at 4 years in FIGARO-DKD). The ESC advised that uptake rates should be substantially lowered.

Parameter	Value applied and source	Comment
Total scripts per patient per year	Based on [redacted] scripts per year × 91.7% adherence from the FIDELITY pooled analysis.	It was unclear whether the adherence estimate accounted for dose titrations and dose interruptions in the trials. The use of this estimate was inconsistent with perfect compliance assumed in the economic analysis.
Patient copayment	$16.28[a] average copayment based on PBS/RPBS utilisation of dapagliflozin (item 10011X) from January 2021 to December 2021.	The average copayment was based on a broader diabetes population that may not be applicable to patients with diabetic kidney disease who are likely to be older, with multiple comorbidities. The average copayment is likely to be lower due to a higher proportion of concessional/safety net scripts.

Source: Section 4.1-4.2 (pp146-459) of the submission
Abbreviations: ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; UACR, urinary albumin to creatinine ratio
[a] Corrected during evaluation. There was an error in the average copayment used in the submission that incorrectly attributed a cost of $6.80 rather than $0 to concessional safety net scripts.

6.51 Table 19 presents the estimated use and financial impact of finerenone to the PBS/RPBS.

Table 19: Estimated use and financial impact

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Australian population aged ≥25 years	18,709,376	19,039,349	19,368,835	19,696,209	20,016,227	20,335,156
CKD prevalent population	[1]	[1]	[1]	[1]	[1]	[1]
CKD diagnosis rate	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Patients diagnosed with CKD	[2]	[2]	[2]	[2]	[2]	[2]
CKD patients with comorbid diabetes and potassium <5 mmol/L (73%)	[3]	[4]	[2]	[2]	[2]	[2]
Patients on ACEi/ARB (80%)	[5]	[6]	[3]	[4]	[2]	[2]
CKD patients with diabetes who meet UACR and eGFR criteria (18%)	[7]	[7]	[7]	[7]	[7]	[8]
Uptake[a]	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Patients treated with finerenone	[9]	[10]	[11]	[12]	[13]	[14]
Total scripts	[8]	[15]	[16]	[17]	[4]	[2]
Cost to PBS/RPBS	$[18]	$[19]	$[20]	$[21]	$[22]	$[23]
Patient copayment [b]	-$[24]	-$[24]	-$[24]	-$[25]	-$[redacted][25]	-$[25]
Net cost to PBS/RPBS [b]	$[18]	$[19]	$[26]	$[20]	$[21]	$[22]

Source: Sections 4.1-4.3 (pp146-159) of the submission
Abbreviations: ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; UACR, urinary albumin to creatinine ratio
[a] Accounts for treatment discontinuations due to death and initiation of renal replacement therapies in the prevalent population
[b] Corrected during the evaluation. There was an error in the average copayment used in the submission that incorrectly attributed a cost of $6.80 rather than $0 to concessional safety net scripts.
The redacted values correspond to the following ranges:
[1] 2,000,000 to < 3,000,000
[2] 1,000,000 to < 2,000,000
[3] 800,000 to < 900,000
[4] 900,000 to < 1,000,000
[5] 600,000 to < 700,000
[6] 700,000 to < 800,000
[7] 100,000 to < 200,000
[8] 200,000 to < 300,000
[9] 20,000 to < 30,000
[10] 30,000 to < 40,000

[11] *40,000 to < 50,000*
[12] *60,000 to < 70,000*
[13] *70,000 to < 80,000*
[14] *90,000 to < 100,000*
[15] *400,000 to < 500,000*
[16] *500,000 to < 600,000*
[17] *700,000 to < 800,000*
[18] *$20 million to < $30 million*
[19] *$30 million to < $40 million*
[20] *$50 million to < $60 million*
[21] *$60 million to < $70 million*
[22] *$80 million to < $90 million*
[23] *$100 million to < $200 million*
[24] *$0 to < $10 million*
[25] *$10 million to < $20 million*
[26] *$40 million to < $50 million*

6.52 The estimated net cost to the PBS/RPBS for finerenone was $20 million to < $30 million in Year 1, increasing to $80 million to < $90 million in Year 6, a total of $200 million to < $300 million over the first 6 years of listing (original uncorrected estimate $200 million to < $300 million).

6.53 Overall, the approach used in the submission did not adequately identify the pool of patients who would be eligible for treatment with finerenone. Eligible population estimates were inappropriately based on a prevalent pool of CKD patients rather than patients with diabetic kidney disease. The majority of subsequent inputs used to determine the eligible population were also based on the broader CKD population (CKD diagnosis rate, proportion with serum potassium <5 mmol/L, patients on ACEi/ARB) that are unlikely to be applicable to the subgroup of patients with CKD who have a primary diagnosis of diabetes. The ESC advised that CKD diagnosis among patients with diabetes is likely to be higher compared to a non-diabetic CKD patient population.

6.54 In 2011-12, the total prevalence of adults with diabetic kidney disease was 1.7% (comprising 1.1% with cardiovascular disease, diabetes and CKD and 0.6% with diabetes and CKD only) (AIHW 2014 report). This represents approximately 358,402 Australians in Year 1 of listing (calculated as 1.7% × 21,082,471 projected Australian population age ≥18 years in 2023, ABS 3222.0). The ESC considered that the size of the eligible diabetic kidney disease population who are also treated with ACEi/ARB, do not have serum potassium levels greater than 5 mmol/L and have persistent albuminuria is likely to be substantially smaller than estimated in the submission.

6.55 The submission acknowledged that SGLT2 inhibitors are likely to be considered as part of standard of care but did not consider the potential impact of greater use of these agents on the uptake of finerenone. SGLT2 inhibitors and GLP1 analogues (in combination with metformin) are expected to reduce cardiorenal complications, therefore the proportion of patients who require an additional treatment for renal complications is likely to be lower with current standard of care.

6.56 Treatment utilisation estimates may be overestimated based on assumed uptake rates that were meant to account for discontinuations due to death or commencement of

renal replacement therapy. The ESC considered that the uptake rates appeared high when considering discontinuation rates observed in the trials at 4 years (30-40% in FIDELIO-DKD, FIGARO-DKD and FIDELITY). Uptake rates in the PBS population are highly uncertain as it will depend on patient characteristics which were inadequately described in the submission.

6.57 The submission did not consider the potentially substantial proportion of patients with diabetic kidney disease who have comorbid heart failure and/or treatment-resistant essential hypertension for which steroidal mineralocorticoid receptor antagonists (e.g. spironolactone, eplerenone) are recommended treatment options. The ESC considered that the potential displacement of these therapies could be managed via restriction criteria that explicitly exclude patients on other MRAs or patients with established HFrEF and an indication for an MRA.

6.58 The submission did not account for additional costs associated with the monitoring and treatment of hyperkalaemia. The approach was also inconsistent with the economic analysis of the submission, which included additional costs due to hyperkalaemia events with and without hospitalisation. The ESC agreed with the PSCR that Australian clinicians are generally well versed in the monitoring and management of hyperkalaemia, but considered that additional costs in monitoring and management would ensue.

Financial Management – Risk Sharing Arrangements

6.59 The submission stated that the sponsor is willing to work with the Department of Health to managing uncertainty in the financial impact of listing finerenone on the PBS/RPBS through available mechanisms, including but not limited to a review of the proposed clinical criteria and/or a risk-sharing arrangement. The ESC noted the high and uncertain estimated impact on PBS expenditure and advised that the PBAC consider appropriate risk-sharing arrangements. The pre-PBAC response stated the sponsor was willing to consider a risk-sharing arrangement in order to manage any remaining uncertainty in the financial estimates.

For more detail on PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

7.1 The PBAC did not recommend the PBS listing of finerenone for the treatment of diabetic kidney disease. The PBAC had low confidence (due to imprecision and heterogeneity) in the clinical evidence presented for finerenone, particularly in the incremental benefit achieved over and above standard of care (including ACEi/ARB and SGLT2 treatment). It also considered that finerenone had a more limited role in clinical practice than had been suggested by the submission and would be restricted to those who were intolerant to SGLT2 inhibitors, or who had persistent proteinuria despite SGLT2 inhibitor (and ACEi/ARB) treatment. The PBAC considered the economic model was unreliable, and had likely underestimated the incremental cost-

effectiveness ratio, which appeared to be well above that previously accepted for similar conditions.

7.2 The PBAC noted the consumer comments and sponsor hearing described the ongoing need for more effective treatments for diabetic kidney disease, however the PBAC considered that the modest treatment effect seen with finerenone would be expected to only marginally address this need.

7.3 The submission positioned finerenone as an additional line of therapy after lifestyle advice, ACEi or ARB treatment (unless contraindicated) and standard diabetes management in patients with diabetic kidney disease who have persistent high-to-very high albuminuria levels. The PBAC noted that the 2022 American Diabetes Association Chronic Kidney Disease Guidelines positioned finerenone as a treatment option in patients who are at increased risk of cardiovascular events or chronic kidney disease progression or are unable to use an SGLT2 inhibitor, with similar positioning in the draft KDIGO 2022 guidelines. The PBAC recalled that it had accepted the effectiveness of dapagliflozin for CKD at its March 2022 meeting. The PBAC also noted that the treatment effects were limited in patients with less than very high albuminuria (discussed below). In view of this, the PBAC considered that finerenone likely had a more limited place in therapy for use in patients with very high albuminuria (urinary albumin-to-creatinine ratio (UACR) of 300 mg/g (33.9 mg/mmol) or greater), excluding patients with heart failure with reduced ejection fraction (HFrEF), and as an add-on to standard of care comprising an ACEi or ARB and SGLT2i unless contraindicated.

7.4 The PBAC considered that the nominated comparator of 'standard of care' was appropriate but was inconsistent with current clinical practice as defined in the submission. The PBAC proposed a more restricted definition of standard of care comprising an ACEi or ARB and SGLT2 inhibitor (unless contraindicated), in line with the more limited clinical position proposed above, and a level of albuminuria that was consistent with the recommended CKD listing of dapagliflozin. The PBAC agreed with the submission's arguments that SGLT2 inhibitors were considered part of current standard of care for patients with diabetic kidney disease.

7.5 The primary clinical evidence in the submission was 2 head-to-head randomised double-blind trials of different design (FIDELIO-DKD and FIGARO-DKD) and a pooled analysis of individual patient data from these trials (FIDELITY), comparing finerenone plus standard care with placebo plus standard care. The PBAC noted that FIDELIO-DKD and FIGARO-DKD had different primary endpoints and baseline population characteristics and risk, and that both trials had very low baseline use of SGLT2 inhibitors. This heterogeneity introduced uncertainty to the FIDELITY analysis. The PBAC also noted that the submission had presented a comparison between FIDELITY and the OneNil database as a way of supporting applicability of the trial data to the Australian PBS population, however neither the OneNil database nor the FIDELITY population represented the PBS population of interest (those treated with an SGLT2

inhibitor). Instead, the estimates of finerenone treatment effect in this subgroup relied on a small post hoc subgroup analysis from FIDELITY with discordant and imprecise effects seen in the individual FIDELIO-DKD and FIGARO-DKD (discussed below). Overall, the PBAC had low confidence in the clinical evidence presented for this subgroup. This is also reflected in the design of the CONFIDENCE trial (NCT05254002), a trial currently recruiting to investigate finerenone versus empagliflozin versus combined therapy, which could only be ethically justified if there was equipoise regarding the additive benefit of finerenone to an SGLT2 inhibitor.

7.6 In terms of comparative benefits in the broader FIDELITY population, the PBAC noted treatment with finerenone was associated with a statistically significant reduction in composite time to first renal and first cardiovascular event compared to placebo (see Table 7). It agreed with the ESC's assessment that a claim of modestly superior efficacy was reasonable for the duration of the trials and the broader trial populations, and further noted that the composite risk of renal events in the individual trials was driven by a reduction in patients experiencing a sustained ≥40% relative decrease in eGFR from baseline, rather than a reduction in renal failure or renal death (see Table 6). In addition, whilst the PBAC noted the evaluation comment that the FIDELITY pre-specified subgroup analyses of cardiovascular outcomes did not suggest any major treatment effect modifications, it was concerned that the pre-specified subgroup analyses of renal outcomes suggested little to no treatment benefit was observed for patients with less than very high albuminuria at baseline (<300 mg/g) (see paragraph 6.21). Given this, it advised that the proposed PBS restriction be amended to include a clinical criterion limiting treatment to patients with a UACR of 300 mg/g (33.9 mg/mmol) or greater. Finally, the PBAC considered that the benefits observed in FIDELITY were not well translated to support the size of the comparative gains in the proposed PBS population, given likely different baseline risks between populations as well as uncertain treatment effects in the subgroup of patients treated with an SGLT2 inhibitors.

7.7 The PBAC considered that the magnitude of treatment benefit for patients receiving an SGLT2 inhibitor was highly uncertain due to a small number of patients in the clinical trials receiving this class of drugs (6.7% in FIDELITY), which resulted in imprecise and inconsistent results across the clinical trial subgroup analyses for this group (see Table 8 and Table 9). Given this uncertainty, the PBAC considered that conservative estimates of treatment effect in these patients would be most appropriate.

7.8 In terms of the comparative harms, the PBAC noted that finerenone treatment was associated with a decreased incidence of serious adverse events compared to placebo, but associated with increased treatment-related adverse events and adverse events leading to discontinuation, in particular a significant increase in hyperkalaemia (Table 10). Given that the reduction in serious adverse events was partly driven by a reduction in complications associated with diabetic kidney disease, and that the risk of hyperkalaemia was likely to be greater outside the tightly controlled environment

of a clinical trial, the PBAC did not consider that a claim of comparable safety to placebo was adequately supported.

7.9 The PBAC noted that the submission presented a Markov state-transition cohort model with 24 health states, and that the base case incremental cost-effectiveness ratio (ICER) was revised during the evaluation from $5,000 to < $15,000 to $55,000 to < $75,000 per QALY gained (Table 16). The PBAC considered that the model's optimistic structure and inputs discussed below meant that the alternative base case ICER of $55,000 to < $75,000 remained uncertain and likely underestimated. Furthermore, the PBAC considered that the value proposition at this ICER was not supported, given that it was higher than the range generally accepted for chronic conditions and noting that PBAC had recently recommended dapagliflozin for CKD, which had dominated standard of care in its economic modelling and where the trial data had shown a substantial added benefit in terms of reduction in end-stage kidney disease and death. Although the PBAC had considered the dapagliflozin model was not robust, it had determined that listing would be cost-effective at the price proposed in that sponsor's pre-PBAC response (paragraphs 7.7 and 7.8, dapagliflozin, PSD, July 2021 PBAC Meeting). Therefore, the PBAC concluded that finerenone as an add-on to standard of care including an SGLT2 inhibitor, was unlikely to be cost-effective at a price greater than that accepted for dapagliflozin for CKD.

7.10 The PBAC noted that the economic model was sensitive to a number of inputs and assumptions, including the baseline risk of the modelled patient population, the treatment effects applied, the cost of dialysis, and extrapolation of disease progression, hyperkalaemia events, and treatment discontinuation. The PBAC advised that:

- It was inappropriate for the submission to have derived the baseline risk of the majority of modelled events from the individual patient data for placebo patients in the pooled FIDELITY analysis. The PBAC considered that the proposed PBS population would have a lower underlying baseline risk compared with the placebo patients in the pivotal clinical trials. The PBAC advised that the baseline risk in the economic model be adjusted to reflect the proposed PBS population, including use only in patients with very high albuminuria, and expected use of concomitant SGLT2 inhibitor therapy.
- It was inappropriate for the submission to have assumed independent treatment effects for progression in chronic kidney disease and progression to dialysis, agreeing with the ESC that both treatment effects share a high degree of overlap (the PBAC noted this was adjusted in the evaluation alternative base case in Table 16). The PBAC also noted that the submission assumed no effect modification from SGLT2 inhibitor use. The PBAC considered that the analyses used to support this assertion were imprecise due to the large confidence intervals and assuming no effect modification favoured finerenone. The PBAC further noted that the submission assumed that treatment effect was maintained while on treatment and constructed new composite endpoints for first non-fatal cardiovascular event and subsequent cardiovascular

event. The PBAC considered that these assumptions were not adequately supported by the clinical trial data and overestimated the treatment effect of finerenone.

- The model structure did not appropriately account for the relationship between renal disease progression, risk of hyperkalaemia, and treatment discontinuation, which should have been connected. The PBAC agreed with the ESC advice that treatment discontinuation and hyperkalaemia events in the extrapolated period did not reflect clinical practice where both hyperkalaemia and discontinuation become more likely as renal function impairment progresses.
- The costs applied to the dialysis health state were overestimated as suggested in the ESC advice, and the costs applied in the evaluation alternative base case in Table 16 more accurately reflected current Australian practice.
- The uncertainties associated with the economic model could be managed through a re-specified economic analysis that included more conservative assumptions and a model structure that accurately reflected the relationship between the risk of discontinuation and hyperkalaemia and disease progression. The PBAC further advised that this model would need to reflect the more limited clinical position being proposed for finerenone (see paragraph 7.3).

7.11 The PBAC noted that the submission's approach to the financial estimates was intended to be modelled on that of the dapagliflozin CKD submission (dapagliflozin PSD, November 2021 PBAC meeting). The PBAC considered that this had led to a likely overestimate of the eligible patient population as it agreed with the ESC that diagnosis rates in the broader CKD population are unlikely to be applicable to patients with diabetes who are diagnosed with CKD. Moreover, the estimates did not reflect the more limited clinical position proposed by PBAC for finerenone use following treatment with an ACEi/ARB and SGLT2 inhibitor (unless contraindicated) and in patients with very high albuminuria. The PBAC proposed an alternate approach that estimated the number of patients with diabetes according to the number of individuals receiving medicines for diabetes in Australia. After the consideration of the percentage of patients with UACR >300 mg/g (4.6%, AusDiab study), the percentage of high-risk CKD patients receiving an ACEi or ARB (76%, CKD-FIX trial), the percentage of patients with persistent UACR >300 mg/g (64%, DAPA-CKD trial), and the percentage ineligible due to hyperkalaemia risk (up to 58.8%-61.6% of patients who failed screening in the trials), and then assuming utilisation scenarios between 10% and 50% (worst and best case scenarios), the PBAC considered that the number of treated patients would be substantially lower than had been estimated in the submission.

7.12 The PBAC considered a resubmission for finerenone should address the following issues:

- Update the PBS restriction in line with the more limited clinical position proposed;
- Revise the economic model as outlined in paragraphs 7.9 and 7.10; and
- Present revised financial estimates consistent with paragraph 7.11.

7.13 The resubmission may be lodged at any future standard due date for PBAC submissions using the standard re-entry pathway.

7.14 The PBAC noted that this submission is eligible for an Independent Review.

Outcome:
Not recommended

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

Bayer is disappointed by the PBAC's decision not to recommend Finerenone for the treatment of diabetes kidney disease. Bayer remains committed to working with the PBAC to find a pathway forward to bring this treatment to Australian patients in a timely manner.